

Analysis of the optimality principles responsible for vascular network architectonics

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Abstract

The equivalence of two optimality principles leading to Murray's law has been discussed. The first approach is based on minimization of biological work needed for maintaining the blood flow through the vessels at required level. The second one is the principle of minimal drag and lumen volume. Characteristic features of these principles are considered.

An alternative approach leading to Murray's law has been proposed. For that we model the microcirculatory bed in terms of delivering vascular network with symmetrical bifurcation nodes, embedded uniformly into the cellular tissue. It was shown that Murray's law can be regarded as a direct consequence of the organism capacity for controlling the blood flow redistribution over the microcirculatory beds.

1 Introduction

The great amount of natural systems have highly branching networks. As a evident example of such systems we may regard living tissue where blood supplies the cellular tissue with oxygen, nutritious products, etc. through branching vascular network and at the same time withdraws products resulting from living activities of the cellular tissue. A similar situation takes place in respiratory systems where oxygen reaches small vessels (capillaries) going through the hierarchical system of bronchial tubes. There is a question of what physical principles govern network organization living systems under consideration. In this paper we focus our attention on the analyzes of different known optimal principles of network formation for microcirculatory bed and developing new approach to this problem.

Table 1: Typical parameters of the vessel arrangement of a 13-kg dog, after [30].

Vessel type	Diameter $2a, \mu\text{m}$	Length l, cm	Tissue/Vessel radii, d/a	Arrangement anisotropy*
Primary arteries	300	1.0	30	0.86
Small arteries	100	0.5	20	0.50
Terminal vessels	50	0.2	10	0.37
Arterioles	20	0.1	7	0.25

*measured as $(\pi d^2 l)^{1/3}/l$

2 Analysis of the optimality principles

A microcirculatory bed can be reasonably regarded as a space-filling fractal being a natural structure for ensuring that all cells are serviced by capillaries [31]. The vessel network must branch so that every small group of cells, referred below to as “elementary tissue domain”, is supplied by at least one capillary. Since a typical length of capillaries is about 0.3 to 0.7 mm a vessel network generated by an artery of length of order of 1 to 5 cm should contain a sufficiently large number of hierarchy levels. At zeroth level we meet the host artery and the host vein, the mother and daughter vessels belong to n -th and $(n+1)$ -th levels, respectively, and the last level N comprises capillaries. So at each level n of the vascular network the tissue domain supplied by a given microcirculatory bed as a whole can be approximated by the union of the tissue subdomains whose mean size is about the typical length l_n of the n -th level vessels. Thus, the individual volume of these subdomains is estimated as $V_n \sim l_n^3$ and their total number (as well as the total number of n -th level vessels) is about $M_n \sim V_0/l_n^3$, where V_0 is the total volume of the microcirculatory bed. The higher is the level, the more accurate become the independence of such estimates from the particular details of vessel arrangements. For internal organs they approximately hold also for large vessels of regional circulation. To justify the latter statement we present Table 1 relating the vessel lengths and radii to the radii of the corresponding tissue cylinders, i.e. the cylindrical neighborhood falling on one vessel of a fixed level.

This condition that the vascular network be volume-preserving from one generation to the next gives us immediately the local relation between the characteristic lengths of the vessels: $l_n^3 \approx g l_{n+1}^3$ (here $g = 2$ is the order of the vessel branching node). Whence it follows that $l_n \sim l_0 g^{-n/3}$, where l_0 is the characteristic size of the microcirculatory bed region or, what is practically the same, the length of the host artery.

The following analysis, however, will require a more detailed information about the vascular network architectonics. Namely, we need to know how the vessel radii change at the nodes and the relative arrangement of mother and daughter vessels. Actually here we meet the problem as to what fundamental

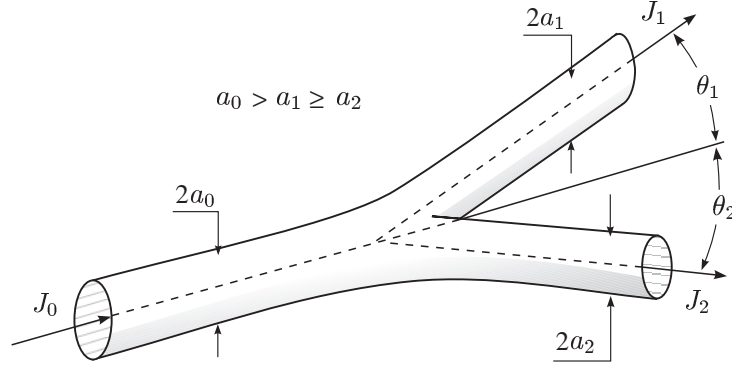


Figure 1: Characteristics of the vessel branching

regularities govern the vessel branching. These regularities manifest themselves in the relation between the radii a_0 , a_1 , a_2 of mother and daughter arteries, respectively, and the angles θ_1 , θ_2 , $\theta_{12} = \theta_1 + \theta_2$ which the daughter branches make with the direction of the mother artery and with each other (Fig. 1).

A detailed theoretical attempt of understanding this regularity was made first by Cecil D. Murray in 1926 [19, 20]. He proposed a model relating the artery radii at branching nodes (Fig. 1) by the expression

$$a_0^x = a_1^x + a_2^x \quad \text{with} \quad x = 3 \quad (1)$$

thereafter referred to as Murray's law (x is also called the bifurcation exponent). Then Murray's approach was under development in a large number of works, see, for example, [1, 2, 22, 29] and a series of works by Zamir *et al.* [36, 37, 40, 41] and by Woldenberg *et al.* [33] (for a historical review see also [28, 40, 12]). The idea of Murray's model is reduced to the assumption that physiological vascular network, subject through evolution to natural selection, must have achieved an optimum arrangement corresponding to the least possible biological work needed for maintaining the blood flow through it at required level. This biological work \mathcal{P} involves two terms: (i) the cost of overcoming viscous drag during blood motion through the vessels obeying Poiseuille's law, and (ii) the energy metabolically required to maintain the volume of blood and the vessel tissue. Dealing with an individual artery of length l and radius a with a blood flow rate J in it we get:

$$\mathcal{P} = \frac{8\eta l J^2}{\pi a^4} + m\pi a^2 l, \quad (2)$$

where η is the blood viscosity and m is a metabolic coefficient. Minimizing function (1) with respect to a we find the relation between the blood flow rate J and the artery lumen radius a corresponding to the given optimality principles:

$$J = ka^3, \quad (3)$$

Table 2: Integral characteristics of the vessel cross-section at different branching levels, after [12].

Vessel type	Mean radius $a, \mu\text{m}$	$\sum a^2$ cm^2	$\sum a^3 \cdot 10$ cm^3	$\sum a^4$ cm^4
<i>Homo sapiens</i>				
Aorta	12500	1.56	1.95	2.44
Arteries	2000	6.36	1.27	0.25
Arterioles	30	127.4	0.382	1.15×10^{-3}
Capillaries	6	1432	0.860	5.16×10^{-4}
Venules	20	1273	2.55	5.09×10^{-3}
Veins	2500	12.9	3.18	0.80
Vena cava	15000	2.25	3.38	5.06
<i>Canis familiaris</i>				
Aorta	5000		1.25	
Large arteries	1500		1.35	
Main arterial branches	500		0.75	
Terminal branches	300		0.486	
Arteriolas	10		0.400	
Capillaries	4		0.768	
Venules	15		2.70	
Terminal veins	750		7.59	
Main venous branches	1200		10.37	
Large veins	3000		10.80	
Vena cava	6250		1.53	

where the coefficient $k = \sqrt{m\pi^2/(16\eta)}$ is a constant for the tissue under consideration. Due to the blood conservation at branching nodes we can write $J_0 = J_1 + J_2$ (Fig. 1) whence Murray's law (1) immediately follows.

However, care must be taken in comparing measurements with prediction, particularly if averages over many successive levels are used. Already Mall himself noted that his data were approximate [17]. In particular, for large arteries of systemic circulation where blood flow can be turbulent the bifurcation exponent x should be equal to $7/3 \approx 2.33$ as it follows from this optimality principle of minimum pumping power and lumen volume.

There is also another optimality principle leading to Murray's law, the principle of minimum drag and lumen surface [36, 37]. The drag against the blood motion through vessels is caused by the blood viscosity and can be described in terms of the shear stress on the walls of vessels, $2\pi a l \tau_t$, where

$$\tau_t = \eta \nabla_n v = \frac{a}{2l} \delta P = \frac{4\eta}{\pi} \frac{J}{a^3} \quad (4)$$

for the laminar flow and δP is the pressure drop along a vessel of length l and radius a . Then the given optimality principle is reduced to the minimum condition for the function

$$\mathcal{P}' = \frac{8\eta l J}{a^2} + m' 2\pi a l, \quad (5)$$

where m' is a certain weighting coefficient. Minimizing (5) with respect to a we get a relationship between J and a of the same form as (3), leading to Murray's law again. There were a number works (see, e.g., [40, 33, 5, 7]) aimed at finding out what the specific optimality principle governs the artery branching by studying the angles of daughter vessels, $\theta_1, \theta_2, \theta_{12}$, in relation to the asymmetry of the branching node, a_2/a_1 (Fig. 1). However, on one hand, all the optimality principles give numerically close relationships between the vessel angles and radii for the bifurcation exponent $x \approx 3$ [33]. On the other hand, it turned out that experimentally determined branching angles generally exhibit considerable scatter around the theoretical optimum. The matter is that small variations of the total "cost" of artery bifurcation about several percents causes the actual vessel angles to deviate significantly from the predicted optimum. This feature is illustrated in Fig. 2 showing the variations in the vessel angles governed by the minimality of functional (5) with imposed 10% perturbations. Namely, varying the coordinates of the branching node (Fig. 1) we get that the minimum of the function $\mathcal{P}'_0 + \mathcal{P}'_1 + \mathcal{P}'_2$ is attained when

$$a_1 \cos \theta_1 + a_2 \cos \theta_2 = (1 + \epsilon) a_0, \quad (6)$$

$$a_1 \sin \theta_1 - a_2 \sin \theta_2 = \epsilon' a_0, \quad (7)$$

where the additional terms ϵa_0 and $\epsilon' a_0$ with $|\epsilon|, |\epsilon'| < 0.1$ describes possible deviations from the optimality condition. The resulting values of θ_1 and θ_2 are depicted in Fig. 2. It should be noted that expressions (6), (7) correspond actually to the mechanical equilibrium of the node under the action of vessel

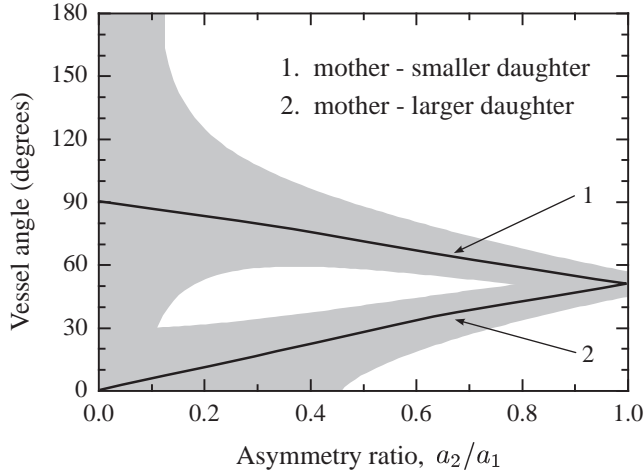


Figure 2: The angles that the daughter arteries make with the mother artery when the vessel branching is governed by the minimum drag & surface principle (solid lines) and under 10% perturbations (darkened region).

walls strained by the blood motion and the additional terms describe a possible effect of the cellular tissue.

Nevertheless, the optimality principles based on functional (2) seems to govern the artery bifurcations [7]. Besides, this principles gives also adequate estimates of the integral characteristics of microcirculatory beds [10, 11].

The bifurcation exponent x , on the contrary, is well approximated by the Murray value, $x \approx 3$, at least starting from arteries of intermediate size [39]. This value meets also the space-filling requirement for the vascular network fractal in geometry to fill precisely the space of a fixed relative volume at each hierarchy level [18]. Indeed, assuming the volume of the tissue cylinders matching an artery of length l and lumen radius a to be about l^3 we get that the corresponding relative volume of blood is $(a/l)^2$. So it is fixed if $a = \text{constant} \cdot l$ and, thus, $a_0^3 = a_1^3 + a_2^3$ provided the tissue cylinder matching the mother artery is composed of the tissue cylinders of the daughter arteries.

In order to specify the microcirculatory bed structure we need also to classify vessels according to the symmetry of their branching (Fig. 3). The matter is that [41] arteries with predominantly asymmetric bifurcations give off comparatively little flow into its side branches along its way and, therefore, able to carry the mainstream flow across larger distances. Conversely, a more symmetric bifurcation pattern splits flow into numerous small branches, thereby delivering blood to its surrounding tissue. Such arteries have been attributed a “conveying” and “delivering” types of function, respectively. Since blood must be conveyed towards the sites at which to be delivered, both types of vessels occur in real arterial trees. Moreover, a larger conveying vessel may switch into

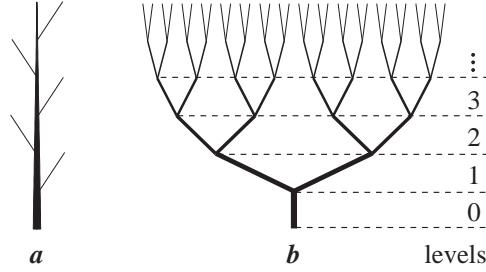


Figure 3: Schematic illustration of the “conveying” (*a*) and “delivering” (*b*) types of artery pattern.

a bunch of small delivering branches.

Obviously, real arterial trees should contain a great variety of intermediate stages in between these extremes and as our field of view moves from the large systemic arteries to small arteries of regional circulation the vessel bifurcation should become more and more symmetrical. This has been also justified by numerically modelling the structure of arterial trees governed by the minimality condition of blood volume [24, 25, 26, 27]. According to the experimental data (see, e.g., the work [5] and Fig. 4 based on it) even sufficiently large regional arteries of diameter and length about $300\ \mu\text{m}$ and $1\ \text{cm}$, respectively, (Table 1) branch symmetrically, at least at first approximation.. Therefore microcirculatory beds as they have been specified above can be regarded as a vessel network with approximately symmetrical bifurcations.

In other words, we may think of the systemic arteries as vessels of the conveying type where the mean blood pressure is practically constant. Conversely, the arteries of microcirculatory beds should belong to the delivering type and mainly determine the total resistance of the vascular network to blood flow, with the blood pressure drop being uniformly distributed over many arteries of different length.

3 Physiological mechanisms governing the vessel arrangements

The universality of Murray’s law for distributed transport systems in many different live organisms raises questions as to: What cues are available to organisms to use in generating such systems? What physiological mechanisms enable them to adapt to altering conditions? Do in fact live organisms follow certain global optimality principles?

For Murray’s law (3) the shear stress τ_t is constant (see formula (4)) throughout a given artery system. Rodbard [21] proposed that the shear stress detected by the vessel endothelium leads to the vessel growth or contraction, and Zamir [38] suggested that this leads to the development of Murray’s system as vessels

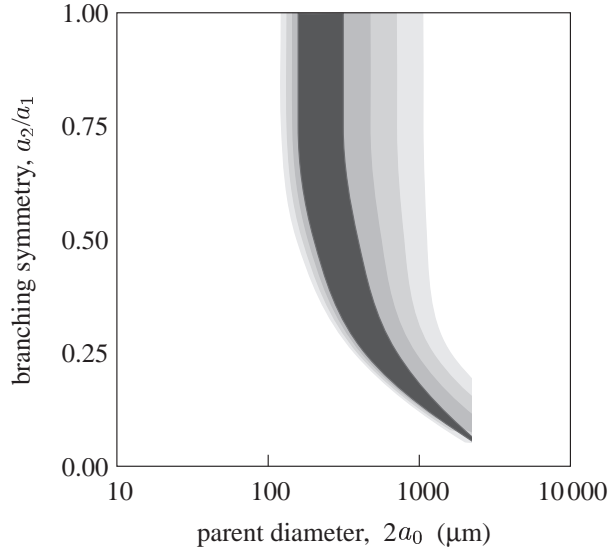


Figure 4: Bifurcation symmetry *vs.* vessel diameter for the porcine coronary arterial tree (based on the data of [5].) The darkness intensity indicates the density of the experimental points.

maintain a constant value of shear stress. Concerning the particular mechanism by which organisms can implement the shear stress sensitivity we can say the following. Now it is established that the adaptation of conduit arteries as well as resistance arteries to acute changes in flow is mediated by the potent endogenous nitrovasodilator endothelium-derived relaxing factor, whose release from endothelial cells is enhanced by flow through the physical stimulation of shear stress (see, e.g., [7] and references therein). The adaptation of arterial diameters to long-term changes in the flow rate also occurs through a mechanism which appears to involve the sensitivity to shear stress and the participation of endothelial cells, but remains not to be understood well [7].

It should be noted that the shear stress equality through a vascular network does not lead directly to a certain optimality principle. Different principles, for instance, (2) and (5), can give the same condition imposed on the shear stress. Moreover, it is quite possible that the case of this equality is of another nature. In particular, for large conduit arteries in the human pulmonary tree the bifurcation exponent x is reported to be in the range 1–2, whereas Murray’s law holds well beginning from intermediate conveying arteries [34, 13]. The matter is that in large systemic arteries the blood pressure exhibits substantial oscillations because of the heart beating, giving rise to damped waves travelling through the systemic arteries. The value of the bifurcation exponent $x = 2$ matching the area-preserving law at the branching nodes ensures that the energy-carrying waves are not reflected back up the vessels at the nodes. How-

ever, this requirement is also can be derived from a certain optimality principle [31].

Summarizing the aforesaid we will model the microcirculatory bed in terms of a delivering vascular network with symmetrical bifurcation nodes embedded uniformly into the cellular tissue. Besides, the Murray's law will be assumed to hold. The latter is also essential from the standpoint of the tissue self-regulation, which will be discussed in detail in the next section. Here, nevertheless, we make several remarks concerning the given aspect too, because it could be treated as an alternative origin of Murray's law (3). Let us consider a symmetrical dichotomous vessel tree shown, e.g., in Fig. 3b. In order to govern blood flow redistribution over the microcirculatory bed finely enough so to supply with, for example, increased amount of blood only those regions where it is necessary and not to disturb other regions the blood pressure should be uniformly distributed over the microcirculatory bed, at least, approximately.

The blood pressure drop δP_n along an artery of level n ($n = 0, 1, 2, \dots$, Fig. 3) for laminar blood flow is

$$\delta P_n = \frac{8\eta l_n J_n}{\pi a_n^4}. \quad (8)$$

For the space-filling vascular network this artery supplies with blood a tissue region of volume about l_n^3 and, so, under normal conditions the blood flow rate J_n in it should be equal to $J_n \approx j l_n^3$, where j is the blood perfusion rate (the volume of blood flowing through a tissue domain of unit volume per unit time) assumed to be the same at all the points of the given microcirculatory bed. Then formula (8) gives us the estimate

$$\delta P_n = \frac{8\eta j}{\pi} \left(\frac{l_n}{a_n} \right)^4$$

whence it follows that δP_n will be approximately the same for all the levels, i.e. the blood pressure will be uniformly distributed over the arterial bed if the ratio l_n/a_n takes a certain fixed value, $l_n \approx \text{constant} \cdot a_n$ and, thus, $J_n \approx \text{constant}' \cdot a_n^3$. Due to the blood conservation at branching nodes we can write

$$J_0 = J_1 + J_2 \quad (9)$$

(see Fig. 1). The later gives us immediately Murray's law (1). In other words, Murray's law can be also regarded as a direct consequence of the organism capacity for controlling finely the blood flow redistribution over the microcirculatory beds.

It should be noted that in the previous papers [14, 15, 16] we considered in detail the mathematical model for the vascular network response to variations in the tissue temperature on the given network architectonics. We have found that the distribution of the blood temperature over the venous bed aggregating the information of the cellular tissue state allows the living tissue to function properly. We showed that this property is one of the general basic characteristics of various natural hierarchical systems. These systems differ from each other by the specific realization of such a synergetic mechanism only.

References

- [1] Cohn, D. “Optimal systems I: the vascular system”, *Bull. Math. Biophys.*, **16**, pp. 59–74 (1954).
- [2] Cohn, D. “Optimal systems II: the vascular system”, *Bull. Math. Biophys.*, **17**, pp. 219–227 (1955).
- [3] Chernoushko, F. L. “Optimal branching tree structures”, *Appl. Math. Mech. U.S.S.R.*, **41**, pp. 376–383 (1977).
- [4] Chernoushko, F. L. “Optimal branching structures in biomechanics”, *Mech. Compos. Mater. U.S.S.R.*, **16**, pp. 308–313 (1980).
- [5] van Bavel, E. and Spann, J. A. E. “Branching patterns in the porcine coronary arterial tree. Estimation of flow heterogeneity”, *Cir. Res.*, **71**, pp. 1200–1212 (1992).
- [6] Green, H. D. “Circulation: physical principles”, in: *Medical Physics*, O. Grassler, edit. (Year Book Publishers, Chicago, 1944), p. 210.
- [7] Griffith, T.M. and Edwards, D.H. “Basal EDRF activity helps to keep the geometrical configuration of arterial branchings close to the Murray optimum”, *J. Theor. Biol.*, **146**, pp. 545–573 (1990).
- [8] Kamiya, A. and Togawa, T. “Optimal branching structure of the vascular tree”, *Bull. Math. Biophys.*, **34**, pp. 431–438 (1972).
- [9] Kamiya, A., Togawa, T., and Yamamota, A. “Theoretical relationship between the optimal models of the vascular tree”, *Bull. Math. Biophys.*, **34**, pp. 311–326 (1974).
- [10] Khanin, M.A. and Bukharov, I.B. “Optimal arterial blood pressure”, *J. Theor. Biol.*, **148**, pp. 289–294 (1991).
- [11] Khanin, M.A. and Bukharov, I.B. “Optimal structure of the microcirculatory bed”, *J. Theor. Biol.*, **169**, pp. 267–273 (1994).
- [12] LaBarbera, M. “Principles of design of fluid transport systems in zoology”, *Science*, **249**, pp. 992–1000 (1990).
- [13] Li, K.-J. *Comparative Cardiovascular Dynamics of Mammals* (CRC Press, Boca Raton, FL., 1996).
- [14] Lubashevsky, I.A., Gafiyuk, V.V. Cooperative mechanism of self-regulation in hierarchical living systems. e- print. <http://xxx.lanl.gov/abs/adap-org/9808003> (1998) to be published in *SIAM J.Appl.Math.*
- [15] Lubashevsky, I.A., Gafiyuk, V.V. Bioheat transfer. New approach to diffusive type process in hierarchically organized active heterogenous media. (Book to be published).

- [16] Lubashevskii, I.A., Gafiychuk, V.V. A simple model of self-regulation in large natural hierarchical systems. *J.Env. Systems.* - v.23, No.3. p.281-289. (1995).
- [17] Mall, F. P. “Die blut und lymphwege in dunndarm des hundes”, *Abhandlungen der Mathematisch-Physischen Classe der Koniglich Sachsischen Gesellschaft der Wissenschaften*, **14**, pp. 151–200 (1888).
- [18] Mandelbrot, B.B. *The Fractal Geometry of Nature* (Freeman, New York, 1982).
- [19] Murray, C. D. “The physiological principle of minimum work. I. The vascular system and the cost of blood volume”, *Proc. Natl. Acad. Sci. U.S.A.*, **12**, pp. 207–214 (1926).
- [20] Murray, C. D. “The physiological principle of minimum work applied to the angle of branching of arteries”, *J. Gen. Physiol.*, **9**, pp. 835–841 (1926).
- [21] Rodbard, S. “Vascular caliber”, *Cardiology*, **60**, pp. 4–49 (1975).
- [22] Rosen, R. *Optimal principles in biology* (Butterworths, London, 1967).
- [23] Schleier, J. “Der Energieverbrauch in der blutbahn”, *Pflugers Archiv Gesamte Physiol. Menschen Tiere*, **173**, pp. 172–204 (1919).
- [24] Schreiner, W. “Computer generation of complex arterial tree models”, *J. Biomed. Eng.*, **15**, pp. 148–150 (1993).
- [25] Schreiner, W. and Buxbaum, P.F. “Computer-optimization of vascular trees”, *IEEE Trans. Biomed. Eng.*, **40**, pp. 482–491 (1993).
- [26] Schreiner, W., Neumann, M., Neumann, F., and Buxbaum, P.F. “Computer-optimization of vascular trees”, *IEEE Trans. Biomed. Eng.*, **40**, pp. 482–491 (1993).
- [27] Schreiner, W., Neumann, F., Neumann, M., End, A., and Müller, M.R. “Structural quantification and bifurcation symmetry in arterial tree models generated by constrained constructive optimization”, *J. Theor. Biol.*, **180**, pp. 161–174 (1996).
- [28] Sherman, T. F. “On connecting large vessels to small. The meaning of Murray’s law”, *J. Gen. Physiol.*, **78**, pp. 431–453 (1981).
- [29] Shoshenko, K.A., Golub, A.G., Brod, V.I., Barbashina, N.E., Ivanova, S.F., Krivoschapkin, A.L., and Osipov V.V. *Architectonics of the Circulatory Bed* (Nauka Publishers, Novosibirsk, 1982) [in Russian].
- [30] Weinbaum, S., Jiji, L.M., and Lemons, D.E. “Theory and experiment for the effect of vascular microstructure on surface tissue heat transfer - Part I: Anatomical foundation and model conceptualization”. *Trans. ASME J. Biom. Eng.*, **106**, pp. 321–330 (1984).

- [31] West, G. B., Brown, J. H., and Enquist, B. J. “A general model for the origin of allometric scaling laws in biology”, *Science*, **276**, pp. 122–126 (1997).
- [32] Wilde, A. G. “The branching patterns of blood-vessels (a theoretical approach)”, *Z. Morphol. und Anthropol.*, **57**, pp. 41–55 (1965).
- [33] Woldenberg, M.J. and Horsfield, K. “Relation of branching angles to optimality for four cost principles”, *J. Theor. Biol.*, **122**, pp. 187–204 (1986).
- [34] Woldenberg, M.J. and Horsfield, K. “Finding the optimal lengths for three branches at a junction”, *J. Theor. Biol.*, **104**, pp. 301–318 (1983).
- [35] Young, T. “On the functions of the heart and arteries”, *Philos. Trans. Royal Soc. London.*, pp. 1–31 (1809).
- [36] Zamir, M. “Optimality principles in arterial branching”, *J. Theor. Biol.*, **62**, pp. 227–251 (1976).
- [37] Zamir, M. “The role of shear forces in arterial branching”, *J. Gen. Physiol.*, **67**, pp. 213–222 (1976).
- [38] Zamir, M. “Shear forces and blood vessel radii in the cardiovascular system”, *J. Gen. Physiol.*, **69**, pp. 449–461 (1977).
- [39] Zamir, M., Wrigley, S.M., and Langille, B.L. “Arterial bifurcations in the cardiovascular system of a rat”, *J. Gen. Physiol.*, **81**, pp. 325–335 (1983).
- [40] Zamir, M. “The branching structure of arterial trees”, *Comm. Theor. Biol.*, **91**, pp. 15–37 (1988).
- [41] Zamir, M. “Distributing and delivering vessels of the human heart”, *J. Gen. Physiol.*, **91**, pp. 725–735 (1988).